91% over two steps), $[\alpha]^{26}_D$ +47.0° (c = 0.7, $CHCl_3$).

The Diels-Alder reaction of diene **7** with 3-(p-toluenesulfonyl)propiolic acid[12] (3 equiv) proceeded with position specificity at 23 °C for 24 h to give an excellent yield (>95%) of adduct **8** and the C(14) diastereomer in a ratio of 3:1. After epoxidation of the mixture (anhydrous CF_3CO_3H in CH_2Cl_2 containing Na_2HPO_4 at −25 °C for 24 h) and sgc with 2:1 hexane–ether the pure epoxide **9** was obtained in 61–65% yield overall from diene **7**.[13] The p-toluenesulfonyl group of **9** was replaced by tributylstannyl by heating with 3 equiv of tri-n-butyltin hydride with a catalytic amount of azoisobutyronitrile as a free radical initiator in toluene at 95 °C for 12 h to give vinylstannane **10** (84%). Coupling of **10** with vinyl triflate **11**[14] was accomplished by heating with 0.07 equiv of $Pd(OAc)_2$ (but not Pd(0) reagents) and 0.14 equiv of PPh_3 in THF at 70 °C for 15 min to provide **12** in 66% yield. Carbonyl reduction ($NaHB(OMe)_3$, −20 °C, THF, 8 h), chloroacetylation (chloroacetic anhydride and pyridine in CH_2Cl_2 at 23 °C for 30 min), and desilylation (1 equiv of Cl_3CCOOH in 10:1 THF–H_2O at 23 °C for 5 h) transformed **12** into hydroxy diene **13** (82% overall). Reaction of **13** with mercuric trifluoroacetate–HgO in CH_3CN at 23 °C for 24 h followed by treatment with Et_4NCl and sgc effected internal oxymercuration to give a single bridged ether chloromercurial (78%) which underwent the required demercuration reaction with Bu_2SnH_2 (but not Bu_3SnH) in toluene at −78 to 0 °C (81%); chloroacetate cleavage with K_2CO_3–methanol at 23 °C for 10 min and oxidation (pyridinium dichromate in DMF at 23 °C for 30 min) provided keto ether **14** (92%, oil), $[\alpha]^{23}_D$ =24.5° (c = 0.1, $CHCl_3$). Reaction of **14** in 10:1 Ac_2O–CH_2Cl_2 with 1.1 equiv of anhydrous $FeCl_3$ in Ac_2O at −78 °C for 12 h gave after sgc purification the rearranged acetate **15** (83%, oil), $[\alpha]^{23}_D$ −20.5° (c = 1.6, $CHCl_3$).[16] Transformation of **15** to glycinoeclepin was effected by the following sequence: (1) desilylation with HF in CH_3CN buffered with excess pyridine for 45 min at 23 °C, (2) oxidation of primary hydroxyl to formyl with pyridinium chlorochromate–Al_2O_3 in CH_2Cl_2 at 23 °C for 12 h, and (3) oxidation of formyl to carboxyl with sodium chlorite–NaH_2PO_4 in t-BuOH–H_2O at 23 °C for 30 min in the presence of 2-methyl-2-butene (as chlorine scavenger) to give after reaction with CH_2N_2 acetyl glycinoeclepin dimethyl ester (oil, 63% overall), $[\alpha]^{23}_D$ −41.1° (c = 0.36, $CHCl_3$). Saponification of acetyl glycinoeclepin mono- or dimethyl ester with 1:1 dimethoxyethane–1 M aqueous lithium hydroxide at 46 °C for 36 h afforded glycinoeclepin A (**1**) (68%). Synthetic **1** was converted to the p-bromophenacyl ester for comparison with an authentic sample.[17] The synthetic and authentic samples were identical by HPLC, MS, IR, 500-MHz ^1H NMR, and optical rotation measurements.

The synthesis reported herein is considerably shorter and simpler than those previously reported and has the potential to provide adequate amounts of **1** for further research. Noteworthy steps in the synthesis include the enantioselective Michael reaction of **2** and **3a** and the conversions **7** → **8**, **8** → **9**, and **14** → **15**. In addition, it should be noted that the coupling reaction, **10** + **11** → **12**, which did not occur with Stille's conditions (Pd(0) reagents), is unusual and probably occurs by replacement of Bu_3Sn in **10** by XPd and a subsequent Heck-type reaction.[18]

Supplementary Material Available: Full spectral data on compounds **1** and **4**–**15** as well as other synthetic intermediates (13 pages). Ordering information is given on any current masthead page.

(12) Corey, E. J.; Jardine, P. D. S.; Rohloff, J. C. *J. Am. Chem. Soc.* **1988**, *110*, 3672–3673.

(13) The stereochemistry of the epoxidation reaction was established by chemical studies involving lactonization of the carboxylic acid corresponding to the BPS ether **9** as well as by the successful conversion to **1**.

(14) Vinyl triflate **11** was prepared enantioselectively and in excellent yields from 2,2-dimethylcyclohexane-1,3-dione by the following sequence: (1) reduction with Baker's yeast[2a,b] or reduction at −78 °C in toluene with catechol borane in the presence of a catalytic amount of the oxazaborolidine from (*R*)-2-(diphenylhydroxymethyl)pyrrolidine and n-butylboronic acid;[15] (2) silylation with triethylsilyl chloride (TESCl)–imidazole in DMF at 23 °C; (3) formylation (HCOOEt, NaH, THF); and (4) reaction with NaH–THF at 23 °C, cooling to −40 °C, and triflate formation with Tf_2NPh.

(15) Corey, E. J.; Bakshi, R. K. *Tetrahedron Lett.* **1990**, *31*, 611–614.

(16) Lewis acids such as $EtAlCl_2$, Et_2AlCl, $BF_3{\cdot}Et_2O$, or $FeCl_3$ in ether converted **14** to the isomeric ketone by rearrangement of hydrogen instead of carbon. The successful rearrangement of **14** to **15** is probably initiated by transfer of CH_3CO^+ to the epoxide oxygen of **14**.

(17) Generously provided by Profs. A. Murai and T. Masamune, Hokkaido University, to whom we express our warmest gratitude.

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The Large Range of Cr–Cr Quadruple Bond Distances: Structural and Theoretical Analysis

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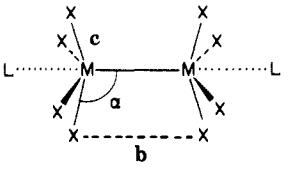
Two aspects of the beautiful conceptual structure of metal–metal multiple bonding[1] remain puzzling; the large variability of the supershort Cr(II)–Cr(II) quadruple bonds, and their response to axial ligation. We present a simple explanation of both phenomena here.

The essential geometrical features of the LX_4MMX_4L system are defined in **1**. We focus on five geometrical parameters; the M–M, M–L, and M–X distances; the "pyramidality" of the MX_4 group, defined by the M–M–X angle α; and the nonbonded X···X distance, which we will call b. In many of the known compounds the latter is fixed as part of a bidentate ligand.



1

Previous efforts to understand the bond-length variations in the system have focused on the distance to the axial ligands L, But look at Figure 1, a plot of the Cr–Cr separation as a function of the pyramidality angle α, for 40 quadruply bonded systems with two, one, or no axial ligands.[2,3] The straight line through these

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(2) The literature references for the compounds plotted are given in the supplementary material.

(3) A few Cr(II) complexes were not included in this analysis: (a) those with a noneclipsed configuration;[4] (b) those having Li^+ ions relatively close to the Cr–Cr bond;[5] and (c) organometallic complexes.[5a,b,6] For a carboxylato compound,[7] the average α is too large because one of the angles is very different from the rest (111° as compared to an average of 99.2°); if this angle is disregarded, the Cr–Cr distance calculated with our least-squares equation is 1.898 Å (experimental value, 1.870 Å).

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(7) Cotton, F. A.; Mott, G. N. *Organometallics* **1982**, *1*, 302.

(8) On the same experimental plot of Figure 1, with no adjustment whatsoever, are superimposed some theoretical points from recent GVB calculations by Davy and Hall: Davy, R. D.; Hall, M. B. *J. Am. Chem. Soc.* **1989**, *111*, 1268. It becomes evident that the difficulties encountered in reproducing theoretically the supershort Cr–Cr bond distances are tied to the small value of α obtained from calculations.

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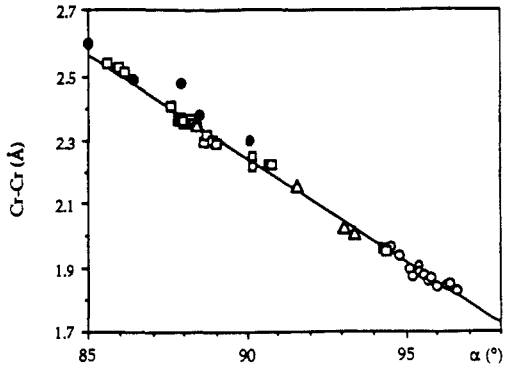
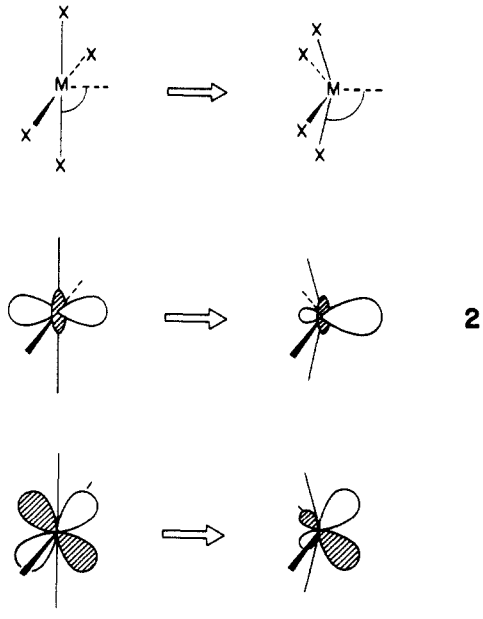


Figure 1. Experimental Cr–Cr bond distances and average pyramidality angles α (**1**) for 40 Cr(II) dinuclear complexes with two (squares), one (triangles), or no (open circles) axial ligands[2] and theoretical results (filled circles) from previous work by Davy and Hall.[8] The straight line Cr–Cr = 8.0588 − 0.0646α) is a least-squares fit of the 40 experimental points.

points has a correlation coefficient $r^2 = 0.995$.

It is pretty clear that the Cr–Cr distance follows the pyramidality over a very large range of distances. Why? In the classical picture of quadruple bonding one has a $\sigma^2\pi^4\delta^2$ configuration. Pyramidalization affects the orbitals involved in the σ and π components of the quadruple bond. In a square-planar ML_4 (α = 90°) complex these are composed of pure metal d_{z^2} and d_{xz}, d_{yz}, respectively, assuming no π bonding with X, as shown in **2**. Upon departure from fragment D_{4h} to C_{4v} symmetry, well-understood mixing (hybridization)[9] with metal $p_{x,y,z}$ orbitals occurs, as indicated on the right side of **2**. The net result is stronger σ and π components of the quadruple bond as α increases from 90°. Extended Hückel calculations bear this out.



2

Addition of an axial ligand should induce, sterically, a decrease in the pyramidality angle α, in the direction of recovering a pseudooctahedral geometry around the Cr atom.[10] Therefore, a direct consequence of the addition of axial ligands should be a weakening of both the σ and π components of the M–M bond.

It would seem as if we have a clear explanation of the large range of bond lengths in these molecules; it is the pyramidality at each center that determines the bond length. But one has to look at certain geometrical constraints operative.

All of the molecules in the correlation of Figure 1 have chelating, bridging carboxylato, amidinato, and related ligands. They have a reasonably similar bite size X···X, around 2.2 Å. In that case the geometrical relationship

$$M\text{–}M = X\cdots X + 2(M\text{–}X)\cos\alpha \qquad (1)$$

holds. Suppose a linear fit, $M\text{–}M = b + 2c\cos\alpha$, is found empirically, as indeed it is in Table I. For constant X···X and M–X in eq 1, that is just what one would expect, and no causal relationship between α and M–M could be drawn. In fact if we fit the available data, b = 2.241 Å and c = 1.854 Å, which are reasonable (the latter a little short) values for X···X and M–X distances.

So how can we then establish a case for the causal primacy of the pyramidality α? One possibility is by seeking such M–M/α correlations across the range of metals; a second is examining unbridged complexes.

Unfortunately, unsupported metal–metal bonded Cr(II) compounds of this type are elusive. Only one is known, with a macrocyclic tetradentate ligand, $[(tmtaa)Cr]_2$.[11] This has Cr–Cr = 2.10 Å at α = 105°, a point that is obviously way off our line. We think that repulsions between the macrocycles simply forbid a short Cr–Cr separation. If the tmtaa were planar, the van der Waals minimum between two such ligands would fix their approach to 3.0–3.5 Å; the shortest metal–metal distance such tetradentate ligands accommodate in other dimers[12] is 3.06 Å.[13] One will have to look for other compounds.

More convincing at this time is the information in Table I. There we summarize structural information on several *families* of triply and quadruply bonded metal complexes, obtained with the help of the Cambridge Structural Database.[14] The following conclusions can be drawn from such data: (a) A strong dependence of M–M on the average value of α (indicated by the slope in the regression equation, $2c$) is found for the carboxylates and analogous compounds of Cr, Mo, and W; (b) for families of compounds of Re and Os with nonbridging ligands, the dependence on α is smaller but still significant, while phosphine complexes of Mo(II) are almost insensitive to changes in α; (c) the fact that the same trend is found for complexes with triple and quadruple metal–metal bonds (Table I) is consistent with the insensitivity of the δ bond to pyramidalization.[10] (d) The slope $2c$ should be equal to 2(M–X) if the geometrical relationship of eq 1 holds. As we noted above, $c \sim$ M–X for Cr. But for all the other compounds c is obviously less than M–X. We take this as evidence that M–M depends on α more fundamentally than through the geometric constraint.

Table I. Least-Squares Parameters for the Equation $M\text{–}M = b + 2c\cos\alpha$, for Several Families of Dinuclear Complexes

metal	ligands	bond order	b	$2c$	no. of compds
Cr	chelates	4	2.241	3.709	40
Mo	chelates	4	2.157	1.739	50
W	chelates	4	2.222	1.922	26
Mo	phosphines	4	2.161	0.101	10
Re	halides	4	2.344	0.474	29
Re	diphosphines	3	2.331	0.297	9
Os	carboxylates	4	2.329	0.511	18

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(13) A theoretical analysis also indicates only a triple bond in this compound: see ref 11b.

(14) Allen, F. H.; Kennard, O.; Taylor, R. *Acc. Chem. Res.* **1983**, *16*, 146.

It is noteworthy that a similar relationship in carbon–carbon bond distances has been found for the family of ethane derivatives, both experimentally and computationally.[15]

In summary, both experimental and theoretical data indicate that there is a correlation between the pyramidality angle and the metal–metal bond distance. Bonding of axial ligands has several effects: competition with the M–M σ bond to be sure, but also steric repulsion of the M–X bonds, which then induces smaller values of α. The small α values, in turn, weaken the M–M bond. This effect may be enhanced by the steric demands of rigid bridging ligands. The interplay of steric and electronic effects in this system is intricate and intriguing.

Acknowledgment. We are indebted to V. Cruz for technical assistance and especially to F. A. Cotton for his thoughtful comments. The research at Barcelona was supported by CICYT through Grant PB86-0272. Collaboration between American and Spanish groups was made possible thanks to a Cooperative Research Grant in Basic Science, CCB86/4004/88, from the U. S.–Spanish Joint Committee for Scientific and Technological cooperation.

Supplementary Material Available: The references for the 40 structures plotted in Figure 1 (3 pages). Ordering information is given on any current masthead page.

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Boron-Containing Nucleic Acids. 2.[1] Synthesis of Oligodeoxynucleoside Boranophosphates

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Received May 29, 1990

Synthetic oligonucleotides are currently attracting considerable attention not only as probes for molecular biology[2] but also as potential therapeutics.[3] For example, oligonucleotides with modified backbones[4] may be used as "antisense" agents to inhibit or control growth of viruses as well as to specifically control the expression of oncogenes or other genes associated with various genetic disorders. Several modifications of the phosphate backbone (see, for example, Figure 1c–e) have been carried out[4a–e] and the modified oligonucleotides have been shown[5] to inhibit the growth of viruses (such as HIV, HSV, etc.) and expression of oncogenes (e.g., c-myc, c-mos).

We now report the first examples of two types of oligonucleotides with a *boronated* internucleotide backbone: the boranophosphates (Figure 1b) and boranophosphate methyl esters (Figure 1f). The boranophosphate species is very closely related to the normal oxygen oligonucleotides (O-oligos, Figure 1a) and the oligonucleotide methylphosphonates (Figure 1c). The boranophosphate methyl esters on the other hand are closely related

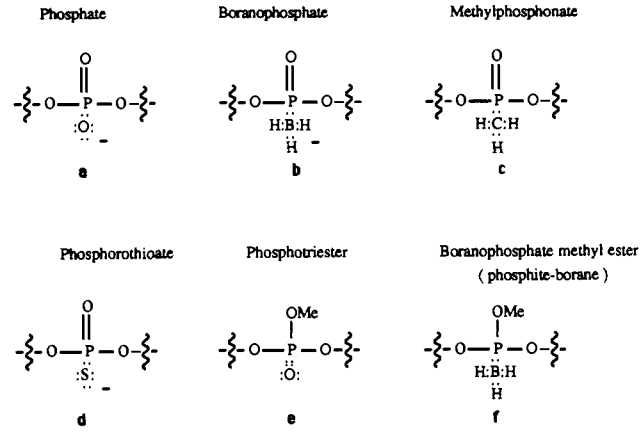
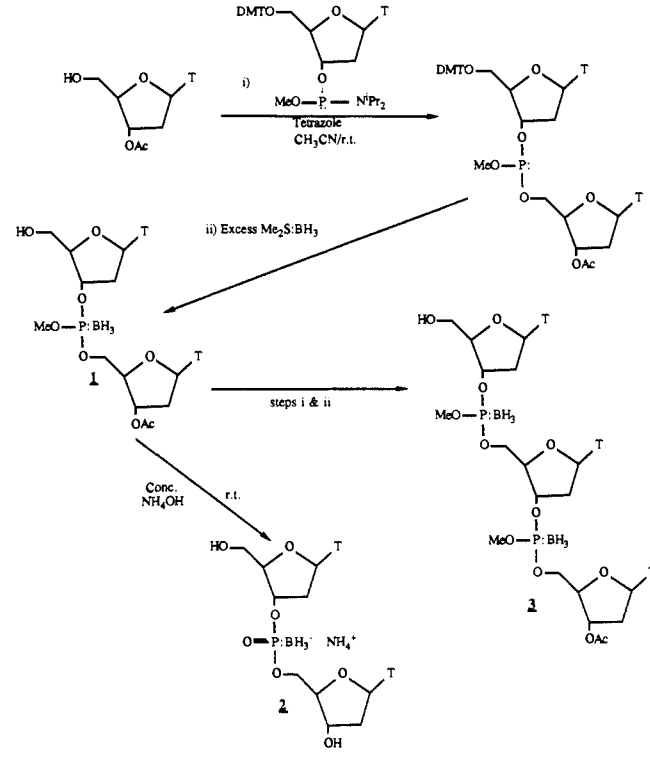


Figure 1. Structurally and/or electronically similar internucleotide linkages: (a) normal phosphate, (b) boranophosphate (borane phosphonate), (c) methylphosphonate, (d) phosphorothioate, (e) phosphotriester, and (f) boranophosphate methyl ester.

Scheme I



† Duke University.
‡ Boron Biologicals, Inc.

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